

CLAIMS

We Claim:

1. A method for detecting the binding of a first member to a second member of a ligand pair, comprising:

- (a) combining a set of first tagged members with a biological sample which may contain one or more second members, under conditions, and for a time sufficient to permit binding of a first member to a second member, wherein said tag is correlative with a particular first member and detectable by non-fluorescent spectrometry or potentiometry;
- (b) separating bound first and second members from unbound members;
- (c) cleaving said tag from said tagged first member; and
- (d) detecting said tag by non-fluorescent spectrometry or potentiometry, and therefrom detecting the binding of said first member to said second member.

2. The method according to claim 1 wherein said first members are bound to a solid support.

3. The method according to claim 2, further comprising, subsequent to the step of separating bound first and second members, washing unbound members from said solid support.

4. The method according to claim 1 wherein the detection of the tag is by mass spectrometry, infrared spectrometry, ultraviolet spectrometry, or, potentiostatic amperometry.

5. The method according to claim 1 wherein greater than 4 tagged first members are combined and wherein each tag is unique for a selected nucleic acid fragment.

6. The method according to claim 1 wherein said bound first and second members are separated from unbound members by a method selected from the group consisting of gel electrophoresis, capillary electrophoresis, micro-channel electrophoresis, HPLC, size exclusion chromatography and filtration.

7. The method according to claim 1 wherein said tagged first members are cleaved by a method selected from the group consisting of oxidation, reduction, acid-labile, base labile, enzymatic, electrochemical, heat and photolabile methods.

8. The method according to claim 4 wherein said tag is detected by time-of-flight mass spectrometry, quadrupole mass spectrometry, magnetic sector mass spectrometry and electric sector mass spectrometry,

9. The method according to claim 4 wherein said tag is detected by potentiostatic amperometry utilizing detectors selected from the group consisting of coulometric detectors and amperometric detectors.

10. The method according to claim 1 wherein steps b, c and d are performed in a continuous manner.

11. The method according to claim 1 wherein steps b, c and d are performed in a continuous manner on a single device.

12. The method according to claim 11 wherein steps b, c and d are automated.

13. The method according to claim 1 wherein said first member is a nucleic acid molecule.

14. The method according to claim 1 wherein said second member is a nucleic acid molecule

15. The method according to claims 13 or 14 wherein said nucleic acid molecule is generated by primer extension.

16. The method according to claims 13 or 14 wherein said nucleic acid molecule is generated from non-3'-tagged oligonucleotide primers.

17. The method according to claims 13 or 14 wherein said nucleic acid molecule is generated from tagged dideoxynucleotide terminators.

18. The method according to claims 13 or 14 wherein said first member is a protein, hormone or organic molecule.

5 19. The method according to claim 18 wherein said protein is selected from the group consisting of antibodies and receptors.

20. A method for analyzing the pattern of gene expression from a selected biological sample, comprising:

- 10 (a) exposing nucleic acids from a biological sample;
(b) combining said exposed nucleic acids with one or more selected tagged nucleic acid probes, under conditions and for a time sufficient for said probes to hybridize to said nucleic acids, wherein said tag is correlative with a particular nucleic acid probe and detectable by non-fluorescent spectrometry or potentiometry;
15 (c) separating hybridized probes from unhybridized probes;
(d) cleaving said tag from said tagged fragment; and
(e) detecting said tag by non-fluorescent spectrometry or potentiometry, and therefrom determining the pattern of gene expression of said biological sample.

20 21. The method according to claim 20 wherein said biological sample is selected from the group consisting of mammalian cells, bacteria and yeast.

22. The method according to claim 21 wherein said mammalian cells contain viruses.

25 23. The method according to claim 20 wherein said exposed nucleic acids is bound to a solid support.

30 24. The method according to claim 23 wherein said solid support is a polymer.

25. The method according to claim 23, further comprising, subsequent to the step of separating, washing the solid support.

35 26. The method according to claim 20 wherein said hybridized probes are separated from unhybridized probes by a method selected from the group

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consisting of gel electrophoresis, capillary electrophoresis, micro-channel electrophoresis, HPLC, filtration and polyacrylamide gel electrophoresis.

27. The method according to claim 20 wherein said tagged probes are
5 cleaved by a method selected from the group consisting of oxidation, reduction, acid-labile, base labile, enzymatic, electrochemical, heat and photolabile methods.

28. The method according to claim 20 wherein said tag is detected by
a method selected from the group consisting of time-of-flight mass spectrometry,
10 quadrupole mass spectrometry, magnetic sector mass spectrometry and electric sector mass spectrometry.

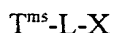
29. The method according to claim 20 wherein said tag is detected by
potentiostatic amperometry utilizing detectors selected from the group consisting of
15 coulometric detectors and amperometric detectors.

30. The method according to claim 20 wherein steps c, d and e are
performed in a continuous manner.

20 31. The method according to claim 20 wherein steps c, d and e are
performed in a continuous manner on a single device.

32. The method according to claim 31 wherein said device is
automated.
25

33. A compound of the formula:



wherein,

30 T^{ms} is an organic group detectable by mass spectrometry, comprising
carbon, at least one of hydrogen and fluoride, and optional atoms selected from
oxygen, nitrogen, sulfur, phosphorus and iodine;

L is an organic group which allows a T^{ms} -containing moiety to be
cleaved from the remainder of the compound, wherein the T^{ms} -containing moiety
comprises a functional group which supports a single ionized charge state when the
35 compound is subjected to mass spectrometry and is selected from tertiary amine,
quaternary amine and organic acid;

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X is MOI other than nucleic acid fragment, and the compound has a mass of at least 250 daltons.

34. A compound according to claim 33 wherein T^{ms} has a mass of
 5 from 15 to 10,000 daltons and a molecular formula of $C_{1-500}N_{0-100}O_{0-100}S_{0-10}P_{0-10}H_{\alpha}F_{\beta}I_{\delta}$
 wherein the sum of α , β and δ is sufficient to satisfy the otherwise unsatisfied
 valencies of the C, N and O atoms.

35. A compound according to claim 33 wherein T^{ms} and L are
 10 bonded together through a functional group selected from amide, ester, ether, amine,
 sulfide, thioester, disulfide, thioether, urea, thiourea, carbamate, thiocarbamate,
 Schiff base, reduced Schiff base, imine, oxime, hydrazone, phosphate, phosphonate,
 phosphoramidate, phosphonamide, sulfonate, sulfonamide or carbon-carbon bond.

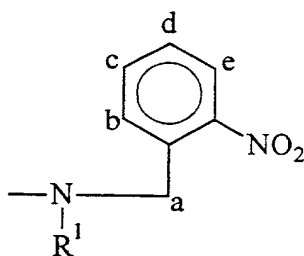
36. A compound according to claim 35 wherein the functional
 15 group is selected from amide, ester, amine, urea and carbamate.

37. A compound according to claim 35 wherein L is selected
 from L^{hu} , L^{acid} , L^{base} , $L^{[O]}$, $L^{[R]}$, L^{enz} , L^{elc} , L^{Δ} and L^{ss} , where actinic radiation, acid,
 20 base, oxidation, reduction, enzyme, electrochemical, thermal and thiol exchange,
 respectively, cause the T^{ms} -containing moiety to be cleaved from the remainder of
 the molecule.

38. A compound according to claim 37 wherein L^{hu} has the
 25 formula $L^1-L^2-L^3$, wherein L^2 is a molecular fragment that absorbs actinic radiation
 to promote the cleavage of T^{ms} from X, and L^1 and L^3 are independently a direct
 bond or an organic moiety, where L^1 separates L^2 from T^{ms} and L^3 separates L^2 from
 X, and neither L^1 nor L^3 undergo bond cleavage when L^2 absorbs the actinic
 radiation.

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39. A compound according to claim 38 wherein $-L^2-L^3$ has the
 formula:



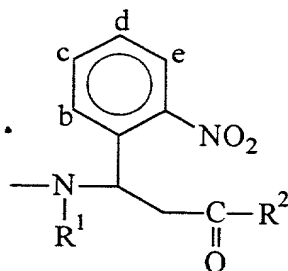
with one carbon atom at positions a, b, c, d or e being substituted with $-L^3-X$ and optionally one or more of positions b, c, d or e being substituted with alkyl, alkoxy, fluoride, chloride, hydroxyl, carboxylate or amide; and R^1 is hydrogen or hydrocarbyl.

40. A compound according to claim 39 wherein X is $\text{---}\overset{\text{O}}{\underset{\text{||}}{\text{C}}}\text{---}R^2$

and R^2 is $-\text{OH}$ or a group that either protects or activates a carboxylic acid for coupling with another moiety.

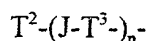
41. A compound according to claim 38 wherein L^3 is selected from a direct bond, a hydrocarbylene, $-\text{O}-$ hydrocarbylene, and hydrocarbylene- $(-\text{O}-\text{hydrocarbylene})_n-\text{H}$, and n is an integer ranging from 1 to 10.

42. A compound according to claim 33 wherein $-L-X$ has the formula:



wherein one or more of positions b, c, d or e is substituted with hydrogen, alkyl, alkoxy, fluoride, chloride, hydroxyl, carboxylate or amide; and R^1 is hydrogen or hydrocarbyl.

43. A compound according to claim 33 wherein T^{ms} has the formula:



5 T^2 is an organic moiety formed from carbon and one or more of hydrogen, fluoride, iodide, oxygen, nitrogen, sulfur and phosphorus, having a mass of 15 to 500 daltons;

T^3 is an organic moiety formed from carbon and one or more of hydrogen, fluoride, iodide, oxygen, nitrogen, sulfur and phosphorus, having a mass of 50 to 1000 daltons;

10 J is a direct bond or a functional group selected from amide, ester, amine, sulfide, ether, thioester, disulfide, thioether, urea, thiourea, carbamate, thiocarbamate, Schiff base, reduced Schiff base, imine, oxime, hydrazone, phosphate, phosphonate, phosphoramidate, phosphonamide, sulfonate, sulfonamide or carbon-carbon bond; and

15 n is an integer ranging from 1 to 50, and when n is greater than 1, each T^3 and J is independently selected.

44. A compound according to claim 43 wherein T^2 is selected from hydrocarbyl, hydrocarbyl-O-hydrocarbylene, hydrocarbyl-S-hydrocarbylene, hydrocarbyl-NH-hydrocarbylene, hydrocarbyl-amide-hydrocarbylene, N-(hydrocarbyl)hydrocarbylene, N,N-di(hydrocarbyl)hydrocarbylene, hydrocarbylacyl-hydrocarbylene, heterocyclylhydrocarbyl wherein the heteroatom(s) are selected from oxygen, nitrogen, sulfur and phosphorus, substituted heterocyclylhydrocarbyl wherein the heteroatom(s) are selected from oxygen, nitrogen, sulfur and phosphorus and the substituents are selected from hydrocarbyl, hydrocarbyl-O-hydrocarbylene, hydrocarbyl-NH-hydrocarbylene, hydrocarbyl-S-hydrocarbylene, N-(hydrocarbyl)hydrocarbylene, N,N-di(hydrocarbyl)hydrocarbylene and hydrocarbylacyl-hydrocarbylene, as well as derivatives of any of the foregoing wherein one or more hydrogens is replaced with an equal number of fluorides.

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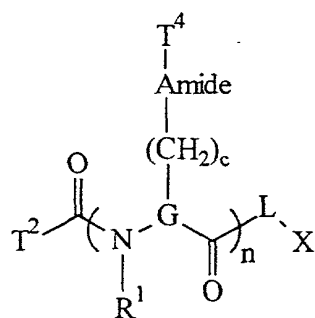
45. A compound according to claim 43 wherein T^3 has the formula $-G(R^2)-$, G is C_{1-6} alkylene having a single R^2 substituent, and R^2 is selected from alkyl, alkenyl, alkynyl, cycloalkyl, aryl-fused cycloalkyl, cycloalkenyl, aryl, aralkyl, aryl-substituted alkenyl or alkynyl, cycloalkyl-substituted alkyl, cycloalkenyl-substituted cycloalkyl, biaryl, alkoxy, alkenoxy, alkynoxy, aralkoxy, aryl-substituted alkenoxy or alkynoxy, alkylamino, alkenylamino or alkynylamino, aryl-substituted alkylamino, aryl-substituted alkenylamino or alkynylamino,

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aryloxy, arylamino, N-alkylurea-substituted alkyl, N-arylurea-substituted alkyl,
 alkylcarbonylamino-substituted alkyl, aminocarbonyl-substituted alkyl,
 heterocyclyl, heterocyclyl-substituted alkyl, heterocyclyl-substituted amino,
 carboxyalkyl substituted aralkyl, oxocarbocyclyl-fused aryl and heterocyclylalkyl;
 5 cycloalkenyl, aryl-substituted alkyl and, aralkyl, hydroxy-substituted alkyl, alkoxy-
 substituted alkyl, aralkoxy-substituted alkyl, alkoxy-substituted alkyl, aralkoxy-
 substituted alkyl, amino-substituted alkyl, (aryl-substituted
 alkyloxycarbonylamino)-substituted alkyl, thiol-substituted alkyl, alkylsulfonyl-
 substituted alkyl, (hydroxy-substituted alkylthio)-substituted alkyl, thioalkoxy-
 10 substituted alkyl, hydrocarbylacylamino-substituted alkyl, heterocyclylacylamino-
 substituted alkyl, hydrocarbyl-substituted-heterocyclylacylamino-substituted alkyl,
 alkylsulfonylamino-substituted alkyl, arylsulfonylamino-substituted alkyl,
 morpholino-alkyl, thiomorpholino-alkyl, morpholino carbonyl-substituted alkyl,
 thiomorpholinocarbonyl-substituted alkyl, [N-(alkyl, alkenyl or alkynyl)- or N,N-
 15 [dialkyl, dialkenyl, dialkynyl or (alkyl, alkenyl)-amino]carbonyl-substituted alkyl,
 heterocyclylaminocarbonyl, heterocyclylalkyleneaminocarbonyl,
 heterocyclylaminocarbonyl-substituted alkyl, heterocyclylalkyleneaminocarbonyl-
 substituted alkyl, N,N-[dialkyl]alkyleneaminocarbonyl, N,N-
 [dialkyl]alkyleneaminocarbonyl-substituted alkyl, alkyl-substituted
 20 heterocyclylcarbonyl, alkyl-substituted heterocyclylcarbonyl-alkyl, carboxyl-
 substituted alkyl, dialkylamino-substituted acylaminoalkyl and amino acid side
 chains selected from arginine, asparagine, glutamine, S-methyl cysteine, methionine
 and corresponding sulfoxide and sulfone derivatives thereof, glycine, leucine,
 isoleucine, allo-isoleucine, tert-leucine, norleucine, phenylalanine, tyrosine,
 25 tryptophan, proline, alanine, ornithine, histidine, glutamine, valine, threonine,
 serine, aspartic acid, beta-cyanoalanine, and allothreonine; alynyl and
 heterocyclylcarbonyl, aminocarbonyl, amido, mono- or dialkylaminocarbonyl,
 mono- or diarylaminoaminocarbonyl, alkylarylaminoaminocarbonyl, diarylaminoaminocarbonyl,
 mono- or diacylaminoaminocarbonyl, aromatic or aliphatic acyl, alkyl optionally
 30 substituted by substituents selected from amino, carboxy, hydroxy, mercapto, mono-
 or dialkylamino, mono- or diarylamino, alkylarylamino, diarylamino, mono- or
 diacylamino, alkoxy, alkenoxy, aryloxy, thioalkoxy, thioalkenoxo, thioalkynoxo,
 thioaryloxy and heterocyclyl.

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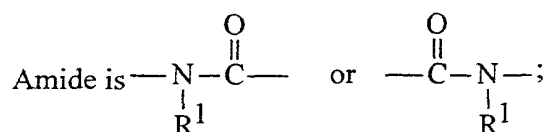
46. A compound according to claim 33 having the formula:



wherein

G is $(CH_2)_{1-6}$ wherein a hydrogen on one and only one of the CH_2 groups is replaced with $-(CH_2)_c\text{-Amide-}T^4$;

- 5 T^2 and T^4 are organic moieties of the formula $C_{1-25}N_{0-9}O_{0-9}H_{\alpha}F_{\beta}$ wherein the sum of α and β is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, and O atoms;



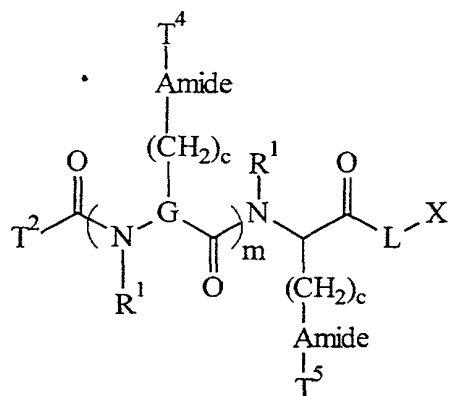
R^1 is hydrogen or C_{1-10} alkyl;

- 10 c is an integer ranging from 0 to 4;

X is defined according to claim 1; and

n is an integer ranging from 1 to 50 such that when n is greater than 1, G, c, Amide, R^1 and T^4 are independently selected.

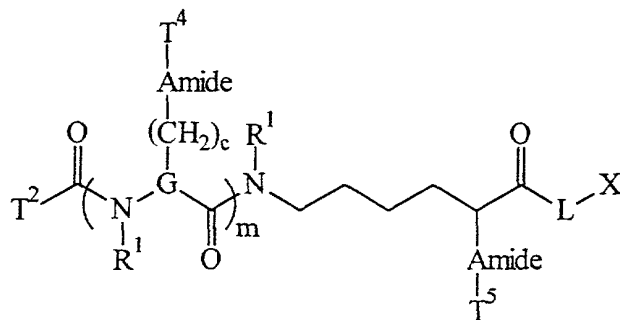
- 15 47. A compound according to claim 33 having the formula: ———



wherein T^5 is an organic moiety of the formula $C_{1-25}N_{0-9}O_{0-9}H_{\alpha}F_{\beta}$ wherein the sum of α and β is sufficient to satisfy the otherwise unsatisfied

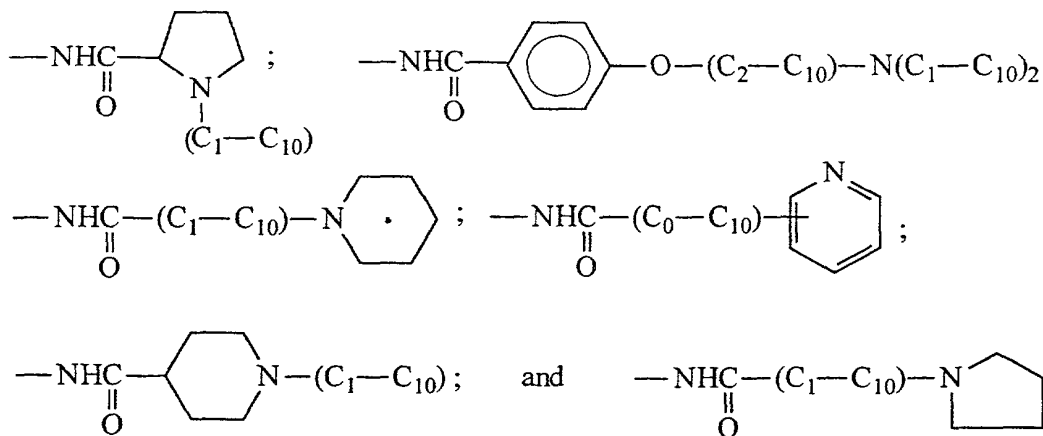
valencies of the C, N, and O atoms; and T⁵ includes a tertiary or quaternary amine or an organic acid; and m is an integer ranging from 0-49.

48. A compound according to claim 33 having the formula:

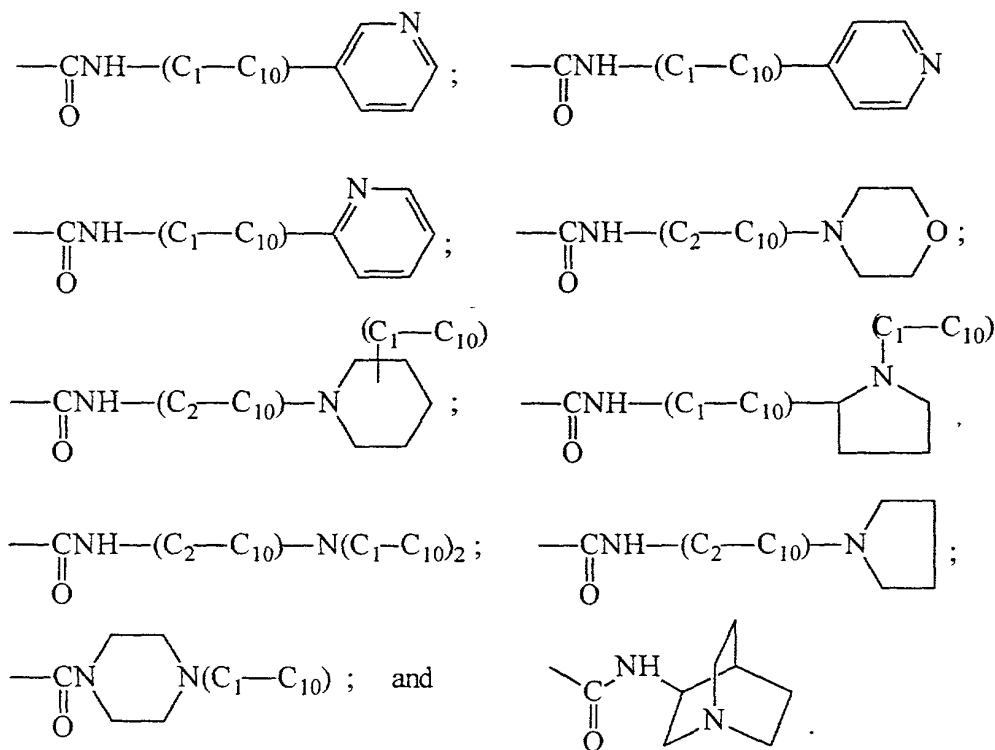


wherein T⁵ is an organic moiety of the formula C₁₋₂₅N₀₋₉O₀₋₉H_αF_β wherein the sum of α and β is sufficient to satisfy the otherwise unsatisfied valencies of the C, N, and O atoms; and T⁵ includes a tertiary or quaternary amine or an organic acid; and m is an integer ranging from 0-49.

49. A compound according to any one of claims 47 and 48 wherein -Amide-T⁵ is selected from:



50. A compound according to any of claims 47 and 48 wherein -Amide-T⁵ is selected from:



51. A compound according to claim 43 wherein T² has the structure which results when one of the following organic acids is condensed with an amine group to form T²-C(=O)-N(R¹)-:
- Formic acid, Acetic acid, Propionic acid,
 - 5 Propionic acid, Fluoroacetic acid, 2-Butynoic acid, Cyclopropanecarboxylic acid, Butyric acid, Methoxyacetic acid, Difluoroacetic acid, 4-Pentynoic acid, Cyclobutanecarboxylic acid, 3,3-Dimethylacrylic acid, Valeric acid, N,N-Dimethylglycine, N-Formyl-Gly-OH, Ethoxyacetic acid, (Methylthio)acetic acid, Pyrrole-2-carboxylic acid, 3-Furoic acid, Isoxazole-5-carboxylic acid, trans-3-
 - 10 Hexenoic acid, Trifluoroacetic acid, Hexanoic acid, Ac-Gly-OH, 2-Hydroxy-2-methylbutyric acid, Benzoic acid, Nicotinic acid, 2-Pyrazinecarboxylic acid, 1-Methyl-2-pyrrolicarboxylic acid, 2-Cyclopentene-1-acetic acid, Cyclopentylacetic acid, (S)-(-)-2-Pyrrolidone-5-carboxylic acid, N-Methyl-L-proline, Heptanoic acid, Ac-b-Ala-OH, 2-Ethyl-2-hydroxybutyric acid, 2-(2-Methoxyethoxy)acetic acid, p-
 - 15 Toluic acid, 6-Methylnicotinic acid, 5-Methyl-2-pyrazinecarboxylic acid, 2,5-Dimethylpyrrole-3-carboxylic acid, 4-Fluorobenzoic acid, 3,5-Dimethylisoxazole-4-carboxylic acid, 3-Cyclopentylpropionic acid, Octanoic acid, N,N-Dimethylsuccinamic acid, Phenylpropionic acid, Cinnamic acid, 4-Ethylbenzoic acid, p-Anisic acid, 1,2,5-Trimethylpyrrole-3-carboxylic acid, 3-Fluoro-4-
 - 20 methylbenzoic acid, Ac-DL-Propargylglycine, 3-(Trifluoromethyl)butyric acid, 1-

- Piperidinepropionic acid, N-Acetylproline, 3,5-Difluorobenzoic acid, Ac-L-Val-OH, Indole-2-carboxylic acid, 2-Benzofurancarboxylic acid, Benzotriazole-5-carboxylic acid, 4-n-Propylbenzoic acid, 3-Dimethylaminobenzoic acid, 4-Ethoxybenzoic acid, 4-(Methylthio)benzoic acid, N-(2-Furoyl)glycine, 2-(Methylthio)nicotinic acid, 3-Fluoro-4-methoxybenzoic acid, Tfa-Gly-OH, 2-Napthoic acid, Quinaldic acid, Ac-L-Ile-OH, 3-Methylindene-2-carboxylic acid, 2-Quinoxalinecarboxylic acid, 1-Methylindole-2-carboxylic acid, 2,3,6-Trifluorobenzoic acid, N-Formyl-L-Met-OH, 2-[2-(2-Methoxyethoxy)ethoxy]acetic acid, 4-n-Butylbenzoic acid, N-Benzoylglycine, 5-Fluoroindole-2-carboxylic acid, 4-n-Propoxybenzoic acid, 4-Acetyl-3,5-dimethyl-2-pyrrolicarboxylic acid, 3,5-Dimethoxybenzoic acid, 2,6-Dimethoxynicotinic acid, Cyclohexanepentanoic acid, 2-Naphthylacetic acid, 4-(1H-Pyrrol-1-yl)benzoic acid, Indole-3-propionic acid, m-Trifluoromethylbenzoic acid, 5-Methoxyindole-2-carboxylic acid, 4-Pentylbenzoic acid, Bz-b-Ala-OH, 4-Diethylaminobenzoic acid, 4-n-Butoxybenzoic acid, 3-Methyl-5-CF₃-isoxazole-4-carboxylic acid, (3,4-Dimethoxyphenyl)acetic acid, 4-Biphenylcarboxylic acid, Pivaloyl-Pro-OH, Octanoyl-Gly-OH, (2-Naphthoxy)acetic acid, Indole-3-butyric acid, 4-(Trifluoromethyl)phenylacetic acid, 5-Methoxyindole-3-acetic acid, 4-(Trifluoromethoxy)benzoic acid, Ac-L-Phe-OH, 4-Pentyloxybenzoic acid, Z-Gly-OH, 4-Carboxy-N-(fur-2-ylmethyl)pyrrolidin-2-one, 3,4-Diethoxybenzoic acid, 2,4-Dimethyl-5-CO₂Et-pyrrole-3-carboxylic acid, N-(2-Fluorophenyl)succinamic acid, 3,4,5-Trimethoxybenzoic acid, N-Phenylanthranilic acid, 3-Phenoxybenzoic acid, Nonanoyl-Gly-OH, 2-Phenoxypyridine-3-carboxylic acid, 2,5-Dimethyl-1-phenylpyrrole-3-carboxylic acid, trans-4-(Trifluoromethyl)cinnamic acid, (5-Methyl-2-phenyloxazol-4-yl)acetic acid, 4-(2-Cyclohexenyloxy)benzoic acid, 5-Methoxy-2-methylindole-3-acetic acid, trans-4-Cotininecarboxylic acid, Bz-5-Aminovaleric acid, 4-Hexyloxybenzoic acid, N-(3-Methoxyphenyl)succinamic acid, Z-Sar-OH, 4-(3,4-Dimethoxyphenyl)butyric acid, Ac-o-Fluoro-DL-Phe-OH, N-(4-Fluorophenyl)glutaramic acid, 4'-Ethyl-4-biphenylcarboxylic acid, 1,2,3,4-Tetrahydroacridinecarboxylic acid, 3-Phenoxyphenylacetic acid, N-(2,4-Difluorophenyl)succinamic acid, N-Decanoyl-Gly-OH, (+)-6-Methoxy- α -methyl-2-naphthaleneacetic acid, 3-(Trifluoromethoxy)cinnamic acid, N-Formyl-DL-Trp-OH, (R)-(+)- α -Methoxy- α -(trifluoromethyl)phenylacetic acid, Bz-DL-Leu-OH, 4-(Trifluoromethoxy)phenoxyacetic acid, 4-Heptyloxybenzoic acid, 2,3,4-Trimethoxycinnamic acid, 2,6-Dimethoxybenzoyl-Gly-OH, 3-(3,4,5-Trimethoxyphenyl)propionic acid, 2,3,4,5,6-Pentafluorophenoxyacetic acid, N-(2,4-Difluorophenyl)glutaramic acid, N-Undecanoyl-Gly-OH, 2-(4-Fluorobenzoyl)benzoic acid, 5-Trifluoromethoxyindole-2-carboxylic acid, N-(2,4-

Difluorophenyl)diglycolamic acid, Ac-L-Trp-OH, Tfa-L-Phenylglycine-OH, 3-Iodobenzoic acid, 3-(4-n-Pentylbenzoyl)propionic acid, 2-Phenyl-4-quinolinecarboxylic acid, 4-Octyloxybenzoic acid, Bz-L-Met-OH, 3,4,5-Triethoxybenzoic acid, N-Lauroyl-Gly-OH, 3,5-Bis(trifluoromethyl)benzoic acid,
 5 Ac-5-Methyl-DL-Trp-OH, 2-Iodophenylacetic acid, 3-Iodo-4-methylbenzoic acid, 3-(4-n-Hexylbenzoyl)propionic acid, N-Hexanoyl-L-Phe-OH, 4-Nonyloxybenzoic acid, 4'-(Trifluoromethyl)-2-biphenylcarboxylic acid, Bz-L-Phe-OH, N-Tridecanoyl-Gly-OH, 3,5-Bis(trifluoromethyl)phenylacetic acid, 3-(4-n-Heptylbenzoyl)propionic acid, N-Hepytanoyl-L-Phe-OH, 4-Decyloxybenzoic acid,
 10 N-(α,α,α -trifluoro-m-tolyl)anthranilic acid, Niflumic acid, 4-(2-Hydroxyhexafluoroisopropyl)benzoic acid, N-Myristoyl-Gly-OH, 3-(4-n-Octylbenzoyl)propionic acid, N-Octanoyl-L-Phe-OH, 4-Undecyloxybenzoic acid, 3-(3,4,5-Trimethoxyphenyl)propionyl-Gly-OH, 8-Iodonaphthoic acid, N-Pentadecanoyl-Gly-OH, 4-Dodecyloxybenzoic acid, N-Palmitoyl-Gly-OH, and N-
 15 Stearoyl-Gly-OH.

52. A compound according to claim 33 wherein MOI is selected from protein, peptide, oligosaccharide, antibody, antigen, drugs and synthetic organic molecules.

53. A composition comprising a pair of compounds of the formula:



wherein,

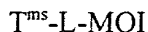
25 T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

30 L is an organic group which allows a T^{ms} -containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms} -containing moiety comprises a functional group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid;

MOI is a nucleic acid fragment wherein L is conjugated to MOI at other than the 3' end of the MOI; and

35 the compounds of the pair have non-identical T^{ms} groups, and have identical sequences except at one base position where the bases are non-identical.

54. A composition comprising a pair of compounds of the formula:



5 wherein,

T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

10 L is an organic group which allows a T^{ms} -containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms} -containing moiety comprises a functional group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid;

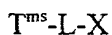
15 MOI is a nucleic acid fragment wherein L is conjugated to MOI at other than the 3' end of the MOI; and

the compounds of the pair have non-identical T^{ms} groups, and have identical sequences except at two base position where the bases are non-identical.

20 55. A composition according to claim any of claims 53 or 54, comprising a plurality of the pairs.

25 56. A composition according to any of claims 53 or 54, comprising a plurality of the pairs, and an equal plurality of non-identical nucleic acids immobilized on a solid support, wherein each member of the plurality of nucleic acids has a base sequence that is exactly complementary to one member of each of the pairs.

30 57. A composition comprising a plurality of compounds having the formula:



wherein,

T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

35 L is an organic group which allows a T^{ms} -containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms} -containing moiety comprises a functional group which supports a single ionized charge state when the

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compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid;

X is MOI excluding a nucleic acid fragment,

and the plurality comprises at least 4 of the compounds, each having

5 non-identical Tms groups.

58. A composition according to claim 57 wherein the plurality is at least 10.

10 59. A kit for mutation analysis comprising a plurality of containers, each container comprising a pair of compounds of the formula:

T^{ms} -L-MOI

wherein,

15 T^{ms} is an organic group detectable by mass spectrometry, comprising carbon, at least one of hydrogen and fluoride, and optional atoms selected from oxygen, nitrogen, sulfur, phosphorus and iodine;

20 L is an organic group which allows a T^{ms} -containing moiety to be cleaved from the remainder of the compound, wherein the T^{ms} -containing moiety comprises a functional group which supports a single ionized charge state when the compound is subjected to mass spectrometry and is selected from tertiary amine, quaternary amine and organic acid; and

MOI is a nucleic acid fragment wherein L is conjugated to MOI at other than the 3' end of the MOI; such that

25 the compounds of each pair have non-identical T^{ms} groups, and have identical sequences except at one or two base position where the bases are non-identical.

60. A kit according to claim 59 wherein the plurality is at least 3.

30 61. A kit according to claim 59 wherein the plurality is at least 5.